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# Oxidation Kinetics of some Amino Acids by 1-Chlorobenzimidazole in Acid Medium – A Kinetic and Mechanistic Approach

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## ABSTRACT

The major product, carboxylic acid, is also revealed in the product review. The oxidation kinetics mechanism proposed is consistent with observed kinetic data. The reactions were monitored potentiometrically up to 70% completion using a platinum-saturated calomel electrode assembly to track the potentials of the reaction mixture containing varying concentrations of the [CBI] / [BI] couple (BI = benzimidazole) at recurring intervals. Using linear plots of log(Et – Eα) versus time, the pseudo-first-order rate constants,k1, were estimated (r0.999)The reactions were found to be first-order, each with respect to [amino acids] and [oxidant]. The rates of the reactions decreases with the added HClO4, and the order in [$HClO_4$] was inverse fractional. The rate of reaction decreases as the dielectric constant of the solvent medium decreases, indicating a dipole-dipole reaction. Electrolytes, such as sodium perchlorate, have little effect on reaction rates. The addition of benzimidazole, one of the reaction ingredients, slowed down the reaction rates. When acrylonitrile was applied to the reaction mixture, no polymerization occurred. The thermodynamic parameters were measured after the kinetic runs were carried out at four different temperatures. The results of the reaction were carboxylic acid, ammonia, and carbon dioxide, according to the report. The most likely reactive species has been identified as HOCl. The observed kinetic effects that have been derived are compatible with a fitting mechanism.

**Keywords:** Amino Acids; CBI; Decarboxylation; Kinetics; Oxidation.

## 1. INTRODUCTION

The chemistry of N-halo compounds forms a separate branch which is of great synthetic importance. (Farook *et al.* 2007). In a recent development, N-halo compounds, the sources of positive halogens, have been extensively employed as oxidizing agents for various organic substrates (Nanda *et al.* 1999; Patrocínio *et al.* 2000; Bandgar *et al.* 2001; Cañibano *et al.* 2001; Dhuru *et al.* 2001). The identity of the oxidising species and reaction mechanism are determined by the halogen atom in nano scale level, the groups attached to the nitrogen atom, and the reaction conditions.

Glycine, alanine, phenylalanine, tryptophan, leucine, and cysteine are amino acids that play an essential role in our biological system and metabolism. These amino acids are used as dietary supplements as well as in biochemical, microbiological, and nutritional research.Oxidation of amino acids by various N-halo compounds such as N-chlorosaccharin (Farook *et al.* 2004a; Farook *et al.* 2004b), N-bromonicotinamide N-chloronictoinamide, N-bromosuccinimide, Chloramine – B, Bromamine-B (Puttaswamy *et al.* 2001) Chloramine-T (Rangappa *et al.* 2002) and N-bromophthalimide (Singh *et al.* 2009a; Singh *et al.* 2009b; Rani *et al.* 2009; Singh *et al.* 2010; Alhaji *et al.* 2011a; Alhaji *et al.* 2011b) have been reported .

The authors have previously demonstrated the oxidative potential of 1-Chlorobenzimidazole (CBI) for a variety of popular reductants, as well as using it to oxidise benzaldehydes, furfural, cyclanols, benzyl alcohols (Rukmangathan *et al.* 2016), aliphatic primary alcohols (Rukmangathan *et al.* 2015) and glycine. A thorough review of the literature shows that no systematic kinetic analysis on the oxidation of amino acids using CBI has been performed to date. In the present investigation, the reaction kinetics of oxidation of amino acids such as glycine, alanine, phenylalanine, tryptophan, leucine, and cysteine with CBI has been studied in an aqueous acetic acid medium.

## 2. MATERIALS & METHODS

### 2.1 Materials

1-Chlorobenzimidazole (CBI) was prepared and purified by the literature method. Acetic acid was purified by the standard method, and the fraction distilling at 118 ºC was collected. Benzimidazole (BDH, Anala) was used as such without purification.

Chromatographically pure amino acids such as glycine, alanine, phenylalanine, tryptophan, leucine, and cysteine were further assayed by the acetous perchloric acid method. All other chemicals are of AnalaR grade from E merck brand.

## 2.2 Kinetic Method

All the standard flasks and the reaction bottles were made up of pyrex glass with joint ground stoppers. The volumetric apparatus, pipettes, burettes, and standard flasks were standardized by usual methods. An electrically operated thermostat with a jumo contact thermometer (West Germany) working in conjunction with an electronic relay maintained temperature accurately with fluctuations; not more than 0.1 ºC was used. The bath liquid was water, and it was covered with a layer of thermocole bits to minimize heat and water loss due to radiation.

#### 2.2.1 Preparation of standard solutions

The standard solution of CBI was prepared by dissolving the required quantity of it in glacial acetic acid and standardized by titrating against sodium thiosulphate solution iodometrically. This standard solution of CBI was found to be invariant in its strength over a period of three months. The solutions of amino acids were prepared by dissolving the required quantity of these in 70% acetic acid and 30% water mixture (v/v).

#### 2.2.2 Kinetic Measurements

All kinetic reactions were carried out under pseudo-first-order conditions, with the [amino acid] [CBI] insolvent method 70 percent (v/v) acetic acid-water medium held at 308K, and the reactions' courses were potentiometrically followed.

The required amounts of amino acid solutions, perchloric acid, and acetic acid-water mixture were pipetted out in a double-walled beaker with an inlet and outlet for circulating water from the thermostat set at the desired level in a standard experiment. To reach the desired temperature, the solution was placed in the beaker for about half an hour. Pipetting out the necessary amount of CBI solution, which had already been thermostated for nearly half an hour, kicked off the reaction. The reaction mixture's overall volume was always 25 mL. A stop-watch was started when half the amount of oxidant was added.

The reaction was followed by setting up a cell

**[Pt|BI$^{(+)}$—CBI||$^{(-)}$SCE]**

made up of the reaction mixture into which the platinum electrode and saturated calomel electrode(SCE) were dipped. The cell's EMF was calculated using an Equip-Tronics Digital potentiometer on a regular basis, while the reaction mixture was constantly stirred with a magnetic stirrer. The linear (r0.999) plots of log (Et- E∞) Vs. Time were used to calculate the pseudo-first-order rate constant, k1.

Where, $E_t$ - potential at time‘t’ and $E_\infty$ - potential at infinity.

Iodometry was used to perform the kinetic run, and the effects came within 2% of each other. Since preliminary results revealed that the rate of oxidation is unaffected by changes in ionic pressure, no effort was made to maintain it stable.

#### 2.2.3. Product analysis and stoichiometry

The stoichiometries of the reactions were determined by the equilibrating varying ratio of [CBI] Vs [amino acid] at 303K for 48 hours under kinetic conditions. Estimation of unconsumed CBI revealed that 2 moles of CBI was required to oxidize 1 mole of the amino acid.

$$2\ CBI + H_2NCH(R)COOH \longrightarrow BI + RCOOH + 2HCl + NH_3 + CO_2$$

where R = $-CH_2 - CH(CH_3)_2$ ; (for example of Leucine)

The reaction mixture from the actual kinetic run after sufficient time was then evaporated with ether. The layer was then separated and dried. Spot tests (Feigl, 1954) and Nessler's reagent confirmed the formation of the resulting carboxylic acid.

## 3. RESULTS & DISCUSSION

Oxidation of amino acids viz. glycine, alanine, phenyl alanine, tryptophan, leucine and cysteine by 1-chlorobenzimidazole has been carried out in 70% (v/v) acetic acid – water medium in the presence of perchloric acid at 308K. In all the cases the corresponding carboxylic acids are the major products. The rates of the reactions were measured by following the disappearance of [CBI] potentiometrically. The reactions were followed under pseudo first order conditions where the concentrations of the amino acids were in large excess compared to that of [CBI].

The oxidation kinetics of all the amino acids by CBI follows the same kinetic trend. For the sake of simplicity, the kinetic results observed for the oxidation of Leucine by CBI have been interpreted.

i. The rate constant values obtained from the integrated first-order equation, the linearity of the log (Et-E∞) Vs time map, and the invariance

of kobs values with differing initial [CBI] all show that the reactions are first-order dependent on [CBI]. (See Table 1 and Fig. 1).

ii. The reaction has a one-to-one correspondence with [amino acid], and kobs is strictly proportional to [amino acid], as shown by the constant values of k2. The relationship between log kobs and log [amino acid] is also linear, with a slope of one (Table 1).

iii. The rate of the reaction is slowed when perchloric acid is added. (See Table.1).The relationship between log kobs and log [H+] is linear, with a -0.45 slope (r = 0.997). This illustrates that the reaction has an inverse fractional order dependency on [H+].

iv. If the dielectric constant of the medium decreases, the rate of oxidation decreases (Table. 1). A plot of log k2 vs 1/D has a negative slope and is linear.This is indicative of the fact that the reaction is of a dipole-dipole type.

v. The rate is slowed when one of the substances, benzimidazole, is added to the reaction mixture first.

vi. The reaction rate is not altered significantly with the addition of nickel chloride, a typical chlorine scavenger.

vii. When acrylonitrite is added to the reaction mixture, no polymerization occurs

viii. Some amino acids, such as glycine, alanine, phenyl alanine, tryptophan, and cysteine, have been oxidised by CBI under similar conditions. The kinetics of all amino acids are identical. (See Table.2).

ix. Activation and thermodynamic parameters have been calculated for all the amino acids. (Table. 3). The reaction rates are governed by the changes in both the enthalpy and entropy of activation. This is further supported by the lower values of Ea. The negative values of $\Delta S^{\#}$ imply the formation of an ionic transition state with an extensive charge separation with a high degree of solvation. Further, the constancy of $\Delta G^{\#}$ values also confirms the unified mechanism for the oxidation reactions of all the amino acids.

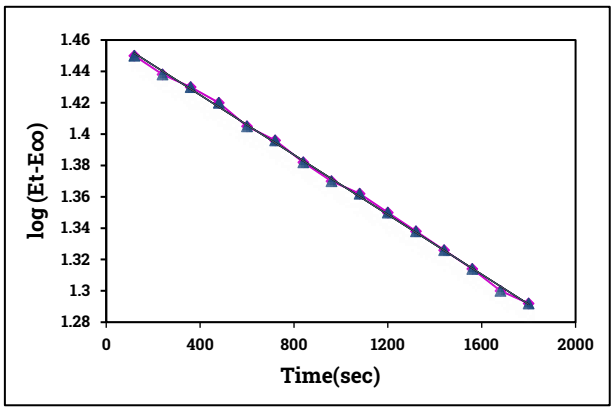


**Fig. 1: First Order Plot of CBI**

**Table 1. Effect of Varying [CBI], [Leucine], [$HClO_4$] and % Acetic Acid**

| [CBI] X $10^3$ mol.$dm^{-3}$ | [leucine] X $10^2$ mol.$dm^{-3}$ | [HClO4] X $10^2$ mol.$dm^{-3}$ | % acetic acid | Kobs X $10^4$ |
|---|---|---|---|---|
| 1.50 | 3.00 | 3.25 | 70 | 5.33 |
| 2.25 | 3.00 | 3.25 | 70 | 5.25 |
| 3.00 | 3.00 | 3.25 | 70 | 5.30 |
| 3.75 | 3.00 | 3.25 | 70 | 5.38 |
| 4.50 | 3.00 | 3.25 | 70 | 5.23 |
| 3.00 | 1.50 | 3.25 | 70 | 2.45 |
| 3.00 | 3.00 | 3.25 | 70 | 5.30 |
| 3.00 | 4.50 | 3.25 | 70 | 7.76 |
| 3.00 | 6.00 | 3.25 | 70 | 10.96 |

| | | | | |
|---|---|---|---|---|
| 3.00 | 7.50 | 3.25 | 70 | 13.80 |
| 3.00 | 3.00 | 1.30 | 70 | 8.91 |
| 3.00 | 3.00 | 3.25 | 70 | 5.30 |
| 3.00 | 3.00 | 5.20 | 70 | 3.98 |
| 3.00 | 3.00 | 7.80 | 70 | 3.09 |
| 3.00 | 3.00 | 9.75 | 70 | 2.83 |
| 3.00 | 3.00 | 3.25 | 60 | 9.72 |
| 3.00 | 3.00 | 3.25 | 70 | 5.30 |
| 3.00 | 3.00 | 3.25 | 80 | 4.23 |
| 3.00 | 3.00 | 3.25 | 90 | 2.94 |

**Table 2. Effect of Amino Acids**

| Amino acid | Glycine | Cysteine | Alanine | Tryptophan | Leucine | Phenyl alanine |
|---|---|---|---|---|---|---|
| kobs $s^{-1}$ $10^4$ | 1.85 | 2.93 | 3.76 | 4.83 | 5.30 | 6.96 |

[CBI] = 3.0 x $10^{-3}$ mol.$dm^{-3}$
[Amino acid] = 3.0 x $10^{-2}$ mol.$dm^{-3}$
[$HClO_4$] = 3.25 ×$10^{-2}$ mol $dm^{-3}$
Solvent = 70% $CH_3COOH$
Temperature = 308 K

The order of reactivity of amino acids with CBI is Phenyl alanine > Leucine > Tryptophan > Alanine > Cysteine > Glycine

(x) Exner plot is found to be linear with the slope value of 1.08 (r = 0.985). The Exner plot's linearity suggests an unified mechanism for CBI oxidation of amino acids (Fig.2). The isokinetic temperature (β) is 217.71K based on the slope of the Exner map. The observed effect of amino acids is real since it is below the laboratory temperature range (298-328K). The value of the slope 'b' of the Exner plot indicates nature of the reaction and selectivity (Table. 4). Since the slope 'b' is greater than one and 217.71 is less than $T_1$ (298K) the experimental data fit the type (3b) of Table. 4. These results indicate an increasing selectivity with an increase in temperature and the reaction series is characterized by compensation effect between $\Delta H^{\#}$ and $\Delta S^{\#}$.

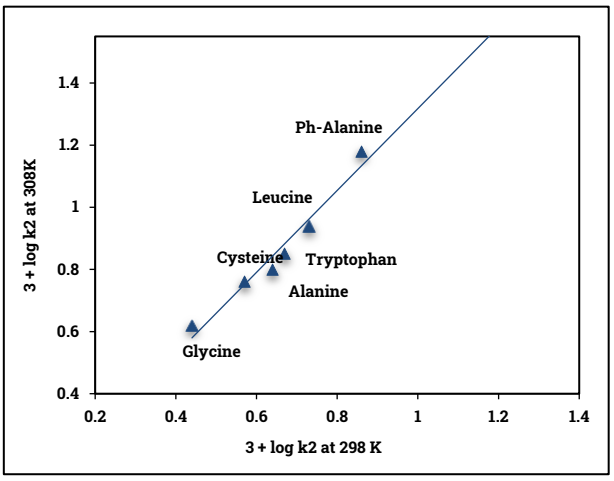


**Fig. 2: Exner Plot of Chosen Amino Acids**

**Table 3. Arrhenius Parameters for the Oxidation of Amino Acids by CBI**

| S. No. | Thermodynamic functions | Amino acids | | | | | |
|---|---|---|---|---|---|---|---|
| | | Glycine | Cysteine | Alanine | Tryptophan | Leucine | Phenyl alanine |
| 1 | $E_a$ kJ mol-1 | 35.05 | 33.87 | 39.63 | 35.70 | 35.70 | 37.64 |
| 2 | $\Delta H^{\#}$ kJ mol-1 | 32.49 | 31.31 | 37.07 | 33.14 | 33.14 | 35.08 |
| 3 | $\Delta G^{\#}$ kJ mol-1 | 97.32 | 96.83 | 97.98 | 98.54 | 98.54 | 97.45 |
| 4 | $-\Delta S^{\#}$ kJ mol-1 | 210.51 | 212.75 | 197.76 | 212.34 | 212.34 | 205.52 |
| 5 | ln A | 5.12 | 5.05 | 5.73 | 5.91 | 5.20 | 5.70 |

**Table 4. Nature of Reaction Series and Selectivity**

| S. No | Characterization | Slope | Selectivity |
|---|---|---|---|
| 1 | log A Constant | T1/T2 - | Decreases |
| 2 | Ea Constant | 1 0 | Unchanged |
| 3a | Compensation effect | <T1/T2 >T2 | Decreases |
| 3b | Compensation effect | >1 <T1 | Increases |
| 3c | Compensation effect | <0 <T2 >T1 | Increases |

## 4. MECHANISM AND RATE LAW

The possible oxidizing species in acidified solution of CBI are $Cl_2$, HOCl, $H_2OCl^+$, $CBIH^+$ and CBI. Molecular chlorine may not be the oxidizing species, since the rate is not influenced by added nickel (II) chloride which is a well-known chlorine scavenger. Since the reaction has a negative dependency on [H+], the presence of CBIH+ as the oxidising species can be ruled out.

Since benzimidazole has a retarding effect, it's possible that the pre-equilibrium stage entails a mechanism in which benzimidazole is one of the components. As a result, HOCl is thought to be the most likely oxidising species in this reaction. Based on the above discussions, the following mechanism has been proposed. The similar kind of mechanism has also been documented in the oxidation of amino acids chloramine–T (Gowda *et al.* 1983), N- bromoacetamide (Bishnoi *et al.* 1985) and N-bromophthalimide (Rani *et al.* 2009; Alhaji *et al.* 2011a) Aldehyde thus formed on further oxidation gives carboxylic acid in excess of oxygen. The mechanism is also supported by the moderate value of energy of activation and other thermodynamic parameters. The following scheme is suggested for the oxidation of leucine by CBI in aqueous acetic acid medium (Fig. 3).

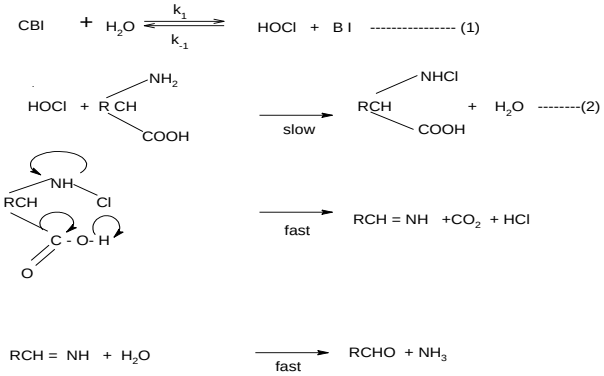


**Fig. 3: The Oxidation of Leucine by CBI in Aqueous Acetic Acid Medium**

## CONCLUSION

The kinetics of 1- chlorobenzimidazole (CBI) oxidation of amino acids in perchloric acid medium specifically reveals that the reaction order is unity with respect to [CBI], [amino acid], and inverse fractional

order with respect to [H+]. The formation of carboxylic acid as the main component is also shown by the product review. The suggested mechanism for oxidation kinetics is consistent with observed kinetic evidence.

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